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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,472	10/04/2005	Masashi Ito	082368-001500US	8056

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 08/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/518,472	ITO ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/4/05 & 5/15/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to papers filed June 9, 2006. Applicant's response to restriction requirement of May 11, 2006 has been entered. Claims 12-16 have been cancelled. No new claims have been added.

Claims 1-11 and 17 are pending in the application.

Election/Restrictions

Applicant's election of Group I (claims 1-11, and 17) without traverse, drawn to a primary cultured adipocyte, wherein the adipocyte stably maintains a foreign gene encoding a protein, and a method of producing said adipocyte for gene therapy, and an implant comprising said adipocytes, is acknowledged. Applicant's election for the species of retroviral vector and insulin genes, is further acknowledged. The requirement for restriction is still deemed proper, maintained and hereby made FINAL.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Applicant timely responded to the restriction (election) requirement in the Paper filed June 9, 2006. Claims 1-11, and 17 are currently under examination.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is unclear. Claim 1 is drawn to an adipocyte for gene therapy that stably maintains a foreign gene encoding a protein. It is not clear how said foreign gene would be expressed in said adipocyte, absent a promoter, or without the context of an expression vector. Further, a gene comprises a genomic locus, and as the specification does not define the term gene, it is not clear whether said adipocyte stably maintains a cDNA for a gene or an entire foreign genomic locus.

Claim 6 is unclear. Claim 6 recites, "primary culturing an adipocyte." Primary culturing is not proper terminology for a method comprising the step of isolating adipocytes and establishing a primary culture. Claim 6 is further unclear in reciting "stably holding", without any reference to where the gene is to be transferred or held. Additionally, the term stably holding is not proper terminology for stably maintaining in the genome. Claim 9 recites "stably holds a foreign gene" and is similarly indefinite.

Claims 2-5 depend from claim 1, claim 7 depends from claim 6, and claims 10-11 depend from claim 9.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1-9 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Furcht et al. (U.S. Patent No. 7,015,037, Provisional Priority to Aug. 5, 1999).

The instant specification defines the term adipocyte as, mature adipocyte and cells comprising the ability to differentiate into adipose tissue, such as preadipocytes...Preadipocytes normally exist as stromal cells that have not yet differentiated (pp. 4-5, bridging).

Furcht et al. teach multipotent adult stem cells that can be maintained in culture in the undifferentiated state, or differentiated to form cells of multiple tissue types, as well as methods for producing the same, for therapeutic use (Abstract). The isolation of the bone marrow derived mononuclear cells is described in Example 1(column 44), and their differentiation into adipocytes is outlined in Example 2 (column 46). The bone marrow derived stem cells are also referred to as mesenchymal stem cells and marrow stromal cells (column 49). Adipocytes derived from the stem cells can be used for the treatment of Type II diabetes (column 25). Furcht et al. specifically describe a number of secreted genes that may be used for gene therapy of diabetes (column 30). Additionally described are viral transfer vectors, including retroviruses (column 32). Retroviral vectors are extensively described in column 35. The transduction of marrow derived stem cells with retroviral vectors encoding eGFP is described in Example 4 (column 48)..

Following *in vitro* culture and gene transfer, the transfected cells may be introduced locally or infused systemically (column 30). Specific examples of engraftment by intramuscular injection or stereotaxic transplantation into mice are described in Example 10 (columns 54-55). Furcht et al. further teach that the genetically altered stem cells can also be encapsulated in an inert carrier to allow the cells to be protected from the host immune system while producing the secreted protein (column 31). A number of pharmaceutically acceptable inert carriers materials, that include polymers and capsules are described in column 31. With specific reference to treatment for diabetes, the authors state that autologous stem cells that have been genetically altered with a retroviral vector to produce insulin at physiologically therapeutic levels can be encapsulated for delivery within the patient's tissues, to produce insulin for extended periods of time (column 31). Furcht et al. further describe stem cells transfected with factor IX, that secrete the protein for at least 8 weeks after infusion into mice (column 30).

Therefore by teaching all the limitations of claims 1-9 and 17, Furcht et al., anticipate the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9-10 and 11 are rejected under 35 U.S.C. §103(a) as being unpatentable over Furcht et al. (U.S. Patent No. 7,015,037, Provisional Priority to Aug. 5, 1999), in view of Crystal et al. (U.S. Patent Publication No: 2002/0076395; filed Dec., 23, 1998), and further in view of Baetge et al. (U.S. Patent No: 5.639.275; filed May 25, 1995).

Furcht et al. describe genetically modified stem cells that may be cultured and differentiated into adipocytes, for gene therapy (Abstract and Examples 1 and 2). Furcht et al. further describe the introduction of secreted insulin by retroviral transduction, followed by encapsulation for implantation, for the treatment of diabetes (column 31). Furcht et al. do not describe their implant composition as further comprising an extracellular matrix component and an angiogenesis factor, but provide the motivation to transfer genetically modified cells secreting insulin in an implant that would ensure successful engraftment and sustained therapeutic release of the secreted protein.

Crystal et al. describe genetically modified adipose tissue comprising an angiogenic substance and expressing a secreted protein, that may be used in the form of an implant (Abstract). Specific examples of angiogenic genes that are also secreted, are described as VEGF and FGF (paragraph [0029], p. 4), transferred to adipocytes by adenoviral vectors (paragraphs [0056-0057], p. 7). The adipose tissue is described as tissue removed from a donor that is treated to increase the vascularity of the adipose tissue implant when it is implanted in the body of the donor, or an immunologically compatible host (paragraph [0069], p. 8).). Crystal et al. do not specifically describe an extracellular matrix component for their implant.

Baetge et al. describe biocompatible capsules for the long-term, stable expression of a biologically active molecule containing genetically engineered cells (Abstract).

Baetge et al. describe hydrogels comprising extracellular matrix components that may be used to form the capsules, to deliver macromolecules, that include insulin (columns 11 and 12). Therefore, it would have been *prima facie* obvious to someone of ordinary skill in the art at the time of the instant invention to include in the implantation method described by of Furcht et al. the extracellular matrix of Baetge et al. together with the angiogenesis factor of Crystal et al. produce an implant composition for *ex vivo* gene therapy of diabetes, comprising primary cultured adipocytes that secrete insulin.

Therefore, a person of ordinary skill in the art, would have been motivated to combine the extracellular matrix of Baetge et al. together with the angiogenesis factor of Crystal et al. to be included in the implant composition described by Furcht et al., because these elements would ensure vascularization and a more stable engraftment for said implant and would have a reasonable expectation of success in producing an implant composition comprising primary adipocytes expressing an insulin gene.

Hence, the claimed invention a whole is *prima facie* obvious, absent evidence to the contrary.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst William Phillips, whose telephone number is **(571) 272-0548**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00 am-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on **(571) 272-0731**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

Fereydoun G. Sajjadi, Ph.D.
Examiner, USPTO, AU 1633

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER